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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/687,528	Applicant(s) STERN ET AL.	
	Examiner Shin-Lin Chen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *7,10 and 17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

1. Claims 7, 10 and 17-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

2. Applicant's election with traverse of group I, claims 1-6, 8, 9 and 11-16, in Paper No. 7 is acknowledged. The traversal is on the ground(s) that group I is not independent from groups II-VIII because they are all drawn to a method for inhibiting new tissue growth in blood vessels, of inhibiting neointimal formation in blood vessels, or preventing exaggerated restenosis in a diabetic subject, and no serious burden is required to search all these groups. This is not found persuasive because of the reasons or record. They are drawn to methods of using different materials having different chemical structures, different physical properties, and different biological functions: polypeptides, organic or inorganic molecules, nucleic acids and antibodies, which have different classifications. Further, they are drawn to methods that differ at least in method steps, reagents and/or dosages used, schedules used, response variables, and criteria for success. A method of inhibiting new tissue growth or neointimal formation or preventing exaggerated restenosis in a subject is different from a method for determining whether a compound inhibits new tissue growth in a blood vessel in a subject, and they differ at least in their objectives, method steps, reagents and/or dosages used, schedules, response variables, and criteria for success.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-24 are pending and claims 1-6, 8, 9 and 11-16 are under consideration.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-6, 8, 9 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims read on administering a polypeptide inhibitor of receptor for advanced glycation endproduct (RAGE) to a subject so as to inhibit new tissue growth or neointimal formation in blood vessels or prevent exaggerated restenosis in a diabetic subject. Claim 6 specifies the inhibitor is a molecule having molecular weight of about 500 daltons to about 100

kilodaltons. The specification only discloses using soluble RAGE, which is a truncated RAGE lacking transmembrane domain, for the claimed method.

The claims encompass a genus of structural variants of soluble RAGE and include various unknown and unidentified polypeptide that may have the same function as soluble RAGE., i.e. inhibitor of RAGE. The genus is highly variant because a significant number of structural differences between genus members is permitted. The various polypeptide inhibitors of RAGE could be totally different from each other and have different structural features. A molecule having molecular weight of about 500 daltons to about 100 kilodaltons encompasses numerous unknown and unidentified polypeptides having unknown biological functions and unknown structures. Therefore, structural features that could distinguish compounds in the genus from others in the polypeptide class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of soluble RAGE is insufficient to describe the genus.

This limited information is not sufficient to reasonably convey to one skilled in the art that applicants were in possession of numerous polypeptide inhibitors of RAGE for the claimed method in the present invention. Thus it is concluded that the written description requirement is not satisfied for the genus.

5. Claims 1-6, 8, 9 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduction of smooth muscle proliferation and migration in carotid artery by treating Fatty Zucker rat with soluble RAGE (sRAGE) via intraperitoneal injection, does not reasonably provide enablement for any method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject any polypeptide inhibitor of RAGE *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to a method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, a polypeptide inhibitor of RAGE, such as sRAGE, *in vivo*. Claim 6 specifies the inhibitor is a molecule having molecular weight of about 500 daltons to about 100 kilodaltons. Claims 11, 12, 14 and 16 specify the administration route of the inhibitor, such as bolus injection, oral administration, i.v., i.p., adenovirus infection etc., or via device, such as a stent or an angioplasty balloon. Claim 13 specifies the inhibitor is administered at a rate of about 2 ug/kg/hr to about 100 ug/kg/hr.

The specification discloses reduction of smooth muscle proliferation and migration in carotid artery by treating Fatty Zucker rat with soluble RAGE (sRAGE) via intraperitoneal injection.

The specification fails to provide adequate guidance and evidence for how to inhibit new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, any polypeptide inhibitor of RAGE other than sRAGE *in vivo*. The claims encompass numerous unknown and unidentified polypeptides having unknown biological functions and unknown structural features, and it is unclear whether these polypeptide could function as inhibitors of RAGE to inhibit new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject *in vivo*.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Rudinger, 1976 (Peptide Hormones, Edited by Parsons, University Park Press, Baltimore, p. 1-7), points out that "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study" (e.g. p. 6). Kaye et al., 1990 (Proc. Natl. Acad. Sci. USA, Vol.

87, pp. 6922-6926) teaches that "A single amino acid substitution results in a retinoblastoma protein defective in phosphorylation and oncoprotein binding" (e.g. Title). Skolnick et al., 2000 (Trends in Biotech, Vol. 18, p. 34-39) states "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for prediction of multiple functional sites. Structural descriptors for protein functional sites are crucial for unlocking the secrets in both the sequence and structural-genomics projects" (e.g. abstract). Skolnick further states that "Knowing a protein's structure does not necessarily tell you its function" and "Because proteins can have similar folds but different functions, determining the structure of a protein may or may not tell you something about its function" (e.g. p. 36, box 2). In view of the lack of detailed information regarding the structural and functional requirements of the polypeptide inhibitor of RAGE, and the unpredictability of polypeptide function from mere amino acid sequence, it would be unpredictable any polypeptide other than sRAGE or polypeptide having a molecular weight of about 500 daltons to about 100 kilodaltons would function as inhibitor of RAGE to inhibit new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject *in vivo*.

Further, claim 16 specifies administering polypeptide inhibitor of RAGE via adenovirus infection. The specification fails to provide adequate guidance for how to administer a polypeptide inhibitor via adenovirus infection. It was known in the art that adenovirus is used for gene transfer, especially in gene therapy, but not for polypeptide transfer. It is unclear how one

skilled in the art would be able to transfer polypeptide inhibitor of RAGE via adenovirus infection *in vivo*.

Therefore, it is concluded that based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, and the breadth of the claims that it would require one skilled in the art at the time of the invention undue experimentation to practice over the full scope of the invention claimed.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4, 6, 8, 9, 11, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Park et al., 1998 (Nature Medicine, Vol. 4, No. 9, p. 1025-1031).

The claims are directed to a method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, a polypeptide inhibitor of RAGE, such as sRAGE, *in vivo*. Claim 6 specifies the inhibitor is a molecule having molecular weight of about 500 daltons to about 100 kilodaltons.

Claims 11 and 16 specify the administration route of the inhibitor, such as bolus injection, oral administration, i.v., i.p., adenovirus infection etc. Claim 15 specifies the subject is suffering from diabetes, acute thrombotic stroke, thrombosis as a result of peripheral vascular surgery etc.

Park teaches advanced glycation endproduct (AGE) engage their receptor in cells of blood vessel wall and activate mechanism linked to the development of vascular lesions. Park teaches soluble extracellular domain of RAGE completely suppresses diabetic atherosclerosis in a glycemia- and lipid-independent manner (e.g. abstract). Park further teaches administering sRAGE, the extracellular two-thirds of the receptor, to a mouse via intraperitoneal injection at a dose of 3 ug/day, 20 ug/day, or 40 ug/day (e.g. p. 1026, right column). The sRAGE has about 318 amino acid residues encoded by 954 nucleotides, and therefore, sRAGE has a molecular weight between about 500 daltons to about 100 kilodaltons (50 kilodaltons MW protein = 1.35 kb DNA). Thus, claims 1-4, 6, 8, 9, 11, 15 and 16 are anticipated by Park.

8. Claims 1, 2, 4, 6, 8, 9, 11, 15 and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Taguchi et al., 2000 (Nature, Vol. 405, p. 354-360).

The claims are directed to a method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, a polypeptide inhibitor of RAGE, such as sRAGE, *in vivo*. Claim 6 specifies the inhibitor is a molecule having molecular weight of about 500 daltons to about 100 kilodaltons.

Claims 11 and 16 specify the administration route of the inhibitor, such as bolus injection, oral administration, i.v., i.p., adenovirus infection etc. Claim 15 specifies the subject is suffering from diabetes, acute thrombotic stroke, thrombosis as a result of peripheral vascular surgery etc.

Taguchi teaches RAGE is a multi-ligand member of the immunoglobulin superfamily of cell surface molecules and interacts with distinct molecules implicated in homeostasis, development and inflammatioin, and certain disease such as diabetes and Alzheimer's disease. Taguchi teaches blocking interaction of RAGE and its ligand amphoterin with sRAGE via intraperitoneal injection into mice decreases growth and metastasis of both implanted tumors and tumors developing spontaneously in susceptible mice (e.g. abstract, p. 355). The sRAGE has about 318 amino acid residues encoded by 954 nucleotides, and therefore, sRAGE has a molecular weight between about 500 daltons to about 100 kilodaltons (50 kilodaltons MW protein = 1.35 kb DNA). Thus, claims 1, 2, 4, 6, 8, 9, 11, 15 and 16 are anticipated by Taguchi.

9. Claims 1-4, 6, 8, 9, 11, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Stern et al., 1998 (WO 98/22138).

The claims are directed to a method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, a polypeptide inhibitor of RAGE, such as sRAGE, *in vivo*. Claim 6 specifies the inhibitor is a molecule having molecular weight of about 500 daltons to about 100 kilodaltons.

Claims 11 and 16 specify the administration route of the inhibitor, such as bolus injection, oral administration, i.v., i.p., adenovirus infection etc. Claim 15 specifies the subject is suffering from diabetes, acute thrombotic stroke, thrombosis as a result of peripheral vascular surgery etc.

Stern teaches a method for treating symptoms of diabetes in a diabetic subject by using agent that inhibits binding of AGE to RAGE, wherein the agent could be polypeptide such as sRAGE and the symptoms comprise abnormal wound healing, symptom of a heart attack, symptoms of a stroke, symptoms of peripheral vascular disease, amputation, symptoms of kidney disease, or inflammation etc (e.g. p. 5, 7, 9, 23). Stern further teaches the subject could be a human, mouse, cow, pig etc., and the administration route of the agent could be intraperitoneal, i.v., intralesional, liposome-mediated delivery, oral, nasal, topical, ocular or otic delivery, and the dose ranges from 200 ng/day/kg to 200,000 ng/day/kg (e.g. p. 7, 24). The sRAGE has about 318 amino acid residues encoded by 954 nucleotides, and therefore, sRAGE has a molecular weight between about 500 daltons to about 100 kilodaltons (50 kilodaltons MW protein = 1.35 kb DNA). Thus, claims 1-4, 6, 8, 9, 11, 15 and 16 are anticipated by Stern.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-3, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern et al., 1998 (WO 98/22138) in view of Nabel et al., 1997 (US Patent No. 5,698,531).

The claims are directed to a method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, a polypeptide inhibitor of RAGE, such as sRAGE, *in vivo*. Claim 12 specifies the device to placed within the subject is a stent of an angioplasty balloon. Claim 13 specifies the inhibitor is administered at a rate from about 2 ug/kg/hr to about 100 ug/kg/hr.

Stern teaches a method for treating symptoms of diabetes in a diabetic subject by using agent that inhibits binding of AGE to RAGE, wherein the agent could be polypeptide such as sRAGE and the symptoms comprise abnormal wound healing, symptom of a heart attack, symptoms of a stroke, symptoms of peripheral vascular disease, amputation, symptoms of kidney disease, or inflammation etc (e.g. p. 5, 7, 9, 23). Stern further teaches the subject could be a

human, mouse, cow, pig etc., and the administration route of the agent could be intraperitoneal, i.v., intralesional, liposome-mediated delivery, oral, nasal, topical, ocular or otic delivery, and the dose ranges from 200 ng/day/kg to 200,000 ng/day/kg (e.g. p. 7, 24).

Stern does not teach using stent or angioplasty balloon to deliver inhibitor or the inhibitor is administered at a rate from about 2 ug/kg/hr to about 100 ug/kg/hr.

Nabel teaches a method of delivering proteins to the walls of the blood vessel or in the tissue perfused by the vessel in a patient via balloon catheter for treating diseases *in vivo* (e.g. abstract).

It would have been obvious for one of ordinary skill at the time of the invention to use balloon catheter as taught by Nabel to deliver the polypeptide inhibitor of RAGE, such as sRAGE, as taught by Stern for the claimed method because both the protein taught by Nabel and the polypeptide inhibitor taught by Stern are both polypeptides and Nabel teaches using balloon catheter to deliver a protein for treating a disease. It would be obvious for one of ordinary skill to substitute one polypeptide with another polypeptide on a ballon catheter. It also would have been obvious for one of ordinary skill at the time of the invention to administer sRAGE at a rate from about 2 ug/kg/hr to about 100 ug/kg/hr because Stern teaches using a dose ranges from 200 ng/day/kg to 200,000 ng/day/kg and determining effective dose is routine optimization of a result-effective variable and is obvious to a person of ordinary skill.

One having ordinary skill at the time the invention was made would have been motivated to administer inhibitor of RAGE via balloon catheter to a patient according to the collective

teachings of Stern and Nabel in order to treat symptoms of diabetes in a diabetic subject, wherein the symptoms comprise abnormal wound healing, symptom of a heart attack, symptoms of a stroke, symptoms of peripheral vascular disease, amputation, symptoms of kidney disease, or inflammation etc., as taught by Stern with reasonable expectation of success.

12. Claims 1-3, 5, 11, 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern et al., 1998 (WO 98/22138) in view of Donovan et al., 1998 (US Patent No. 5,833,651).

The claims are directed to a method for inhibiting new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject, such as a non-human animal, a human, or a transgenic non-human animal, a polypeptide inhibitor of RAGE, such as sRAGE, *in vivo*. Claim 5 specifies the subject has undergone an angioplasty procedure or surgery to implant a stent in a blood vessel. Claim 12 specifies the device to placed within the subject is a stent of an angioplasty balloon. Claim 14 specifies the inhibitor is coated onto a stent used during an angioplasty of the patient.

Stern teaches a method for treating symptoms of diabetes in a diabetic subject by using agent that inhibits binding of AGE to RAGE, wherein the agent could be polypeptide such as sRAGE and the symptoms comprise abnormal wound healing, symptom of a heart attack, symptoms of a stroke, symptoms of peripheral vascular disease, amputation, symptoms of kidney disease, or inflammation etc (e.g. p. 5, 7, 9, 23). Stern further teaches the subject could be a

human, mouse, cow, pig etc., and the administration route of the agent could be intraperitoneal, i.v., intralesional, liposome-mediated delivery, oral, nasal, topical, ocular or otic delivery, and the dose ranges from 200 ng/day/kg to 200,000 ng/day/kg (e.g. p. 7, 24).

Stern does not teach using stent or angioplasty balloon to deliver inhibitor.

Donovan teaches using stent to deliver therapeutic substances, such as viruses, nucleic acids, drugs and therapeutic proteins to a lumen wall of the body for treating or preventing diseases (e.g. column 1, 2).

It would have been obvious for one of ordinary skill at the time of the invention to use stent as taught by Donovan to deliver the polypeptide inhibitor of RAGE, such as sRAGE, as taught by Stern for the claimed method because both the therapeutic protein taught by Donovan and the polypeptide inhibitor taught by Stern are both polypeptides and Donovan teaches using stent to deliver a protein for treating a disease. It would be obvious for one of ordinary skill to substitute one polypeptide with another polypeptide on a stent.

One having ordinary skill at the time the invention was made would have been motivated to administer inhibitor of RAGE via stent, e.g. stent coated with said inhibitor, to a patient according to the collective teachings of Stern and Donovan in order to treat symptoms of diabetes in a diabetic subject, wherein the symptoms comprise abnormal wound healing, symptom of a heart attack, symptoms of a stroke, symptoms of peripheral vascular disease, amputation, symptoms of kidney disease, or inflammation etc., as taught by Stern with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Scott Priebe can be reached on (703) 308-7310. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.

S. Chen